### (19) World Intellectual Property Organization

International Bureau



## : (CERTO CULTURA DE CERTURA DA LO BERTO CORP. DE CONTROL DE CONTROL DE CONTROL DE CONTROL DE CONTROL DE CONTROL

(43) International Publication Date 2 December 2004 (02.12.2004)

**PCT** 

# (10) International Publication Number WO 2004/103348 A3

(51) International Patent Classification?: 31/55, 38/13, 9/14

A61K 9/16,

(21) International Application Number:

PCT/US2004/015621

(22) International Filing Date: 19 May 2004 (19.05.2004)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data: 60/471,581

19 May 2003 (19.05.2003) US

(71) Applicant (for all designated States except US): BAX-TER INTERNATIONAL INC. [US/US]; ONE BAXTER PARKWAY, DEERFIELD, IL 60015 (US).

(72) Inventors; and

- (75) Inventors/Applicants (for US only): BARRETT, Rabinow, E. [US/US]; 9119 Tripp Avenue, Skokie, IL 60076 (US). WERLING, Jane [US/US]; 605 South Highland Avenue, Arlington Heights, IL 60005 (US). KONKEL, Jamie, Teresa [US/US]; 835 Game Trail, Apt. 303, Lakemoor, IL 60050 (US). DOTY, Mark, J. [US/US]; 610 Kenilworth Street, Grayslake, IL 60030 (US). REBBECK, Christine, L. [US/US]; 525 Eagle Ridge Lane, Algonquin, IL 60102 (US).
- (74) Agents: MAYO, Michael, C. et al.; Baxter International Inc., One Baxter Parkway, Deerfield, Illinois 60015 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

#### Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments
- (88) Date of publication of the international search report: 6 January 2005

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: SOLID PARTICLES COMPRISING AN ANTICONVULSANT OR AN IMMUNOSUPPRESSIVE COATED WITH ONE OR MORE SURFACE MODIFIERS

(57) Abstract: This invention pertains to the formulation of small-particle suspensions of anticonvulsants, particularly carbamazepine, for pharmaceutical use. This invention also pertains to the formulation of a small-particle suspensions of immunosuppressive agents, particularly cyclosporin, for pharmaceutical use. The particles are coated with one or more surface modifiers.





onal Application No PCT/US2004/015621

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 A61K9/16 A61K A61K31/55 A61K9/14 A61K38/13 According to International Patent Classification (IPC) or to both national classification and IPC B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) IPC 7 A61K Documentation searched other than minimum documentation to the extent that such documents are included. In the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) EPO-Internal, PAJ, WPI Data, BIOSIS, EMBASE C. DOCUMENTS CONSIDERED TO BE RELEVANT Category \* Citation of document, with indication, where appropriate, of the relevant passages Relevant to daim No. X WO 98/31346 A (MASSACHUSETTS INST 1,2,5,6, TECHNOLOGY; PENN STATE RES FOUND (US)) 9-12,15,23 July 1998 (1998-07-23) 16,29, 30,33, 34,36 claims 1-24 page 8, line 1 - page 22, line 31 χ US 6 387 409 B1 (KHAN SHEEMA ET AL) 1,2, 14 May 2002 (2002-05-14) 5-10,18,19, 23-26, 29-34, 42,43,47 claim 1 table 2 column 2, line 8 - column 3, line 59 Further documents are listed in the continuation of box C. Patent family members are listed in annex. Special categories of cited documents: T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the \*A\* document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "Y" document of particular relevance; the ctaimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled \*O\* document referring to an oral disclosure, use, exhibition or P° document published prior to the international filing date but later than the priority date claimed \*&\* document member of the same patent family Date of the actual completion of the international search Date of mailing of the international search report 21 October 2004 04/11/2004 Name and mailing address of the ISA Authorized officer European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel (+31-70) 340-2040, Tx. 31 651 epo nl. Schifferer, H Fax: (+31-70) 340-3016

li ional Application No PCT/US2004/015621

	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	
ategory *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99/49846 A (RTP PHARMA INC) 7 October 1999 (1999-10-07)  claims 1-10	1,2, 5-10,18, 19, 23-26, 29-34, 42,43,47
	page 3, line 29 - page 5, line 28	
X	US 2003/003155 A1 (REBBECK CHRISTINE L ET AL) 2 January 2003 (2003-01-02)	1-8, 12-16, 18-32, 36-40, 42-47
	claims 1-105 examples 6-9 paragraph '0035! - paragraph '0061!	
X	WO 00/61108 A (BONVOISIN CECILE ISABELLE; LAROCHE CHRISTOPHE (FR); GLAXO GROUP LTD () 19 October 2000 (2000-10-19) claims 1-14 page 4, line 26 - page 6, line 27	25,26, 28,36, 42,43
X	WO 99/53901 A (LOUIS OLIVIER; LLORCA NATHALIE (FR); ROSIER PATRICK (FR); CAVAILLON P) 28 October 1999 (1999-10-28) page 3, line 23 - page 7, line 18 examples 1-5	25-28, 33,36, 37,42,43
X	WO 92/08447 A (GLAXO GROUP LTD) 29 May 1992 (1992-05-29) claims 1-8 page 3, line 25 - page 4, line 24 example 2	25,26, 28,36
	*	

mational application No. PCT/US2004/015621

Box II Observations where certain claims were found unsearchable (Continuation of Item 2 of Irst sheet)
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
Claims Nos.:     because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. Ctaims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)
This International Searching Authority found multiple Inventions in this International application, as follows:
see additional sheet
As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. X As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the Invention first mentioned in the claims; it is covered by claims Nos.:
Remark on Protest  The additional search fees were accompanied by the applicant's protest.  No protest accompanied the payment of additional search fees.

# FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-24

A pharmaceutical composition of an anticonvulsant comprising solid particles of the agent coated with one or more surface modifiers, wherein the particles have an average effective particle size of  $10\ nm-100\ micrometers$ .

2. claims: 25-47

A pharmaceutical composition of an immunosuppressive comprising solid particles of the agent coated with one or more surface modifiers, wherein the particles have an average effective particle size of 10 nm - 100 micrometers

ntormation on patent family members

Int nal Application No PCT/US2004/015621

	nt document n search report		Publication date		Patent family member(s)		Publication date
	<del></del>			110		Λ	05-01-1999
WU 9	831346	Α	23-07-1998	US	5855913 2277801		23-07-1998
				CA	2403349		23-07-1998
				CA	0954282		10-11-1999
				EP	2001526634		18-12-2001
				JP			23-07-1998
				MO	9831346		13-02-2001
				US	RE37053		25-11-2003
				US	6652837		
				US	5985309		16-11-1999
				US	2003068277		10-04-2003
				US	2004062718		01-04-2004
				US	2002052310	A1	02-05-2002
us 6	387409	B1	14-05-2002	US	6337092		08-01-2002
				ΑU	761205		29-05-2003
				AU	3118599	Α	18-10-1999
				CA	2326456		07-10-1999
				CN	1303278	T	11-07-2001
				EP	1067914	A2	17-01-2001
				ĴΡ	2002509876		02-04-2002
				SE	0003429		23-11-2000
				WO	9949846		07-10-1999
	9949846	Α	07-10-1999	AU	761205	R2	29-05-2003
WU S	9949040	^	07-10-1333	AU	3118599		18-10-1999
				CA	2326456		07-10-1999
							11-07-2001
				CN	1303278		17-01-2001
				EP	1067914		
				JP		Ţ	02-04-2002
				SE	0003429		23-11-2000
				MO	9949846		07-10-1999
				US	6387409		14-05-2002
				US	6337092	B1	08-01-2002
US 2	2003003155	A1	02-01-2003	US	2002127278		12-09-2002
				CA	2431705	A1	18-07-2002
				EP	1347747	A2	01-10-2003
				NO	20032860	A	21-08-2003
				WO	02055059	A2	18-07-2002
				ÜS	2003206959	A9	06-11-2003
				US	2003031719		13-02-2003
				US	2003044433		06-03-2003
	•			US	2003100568		29-05-2003
				US	2003096013		22-05-2003
				US	2003072807		17-04-2003
				US	2004022862		05-02-2004
				UJ			14-11-2002
				110	- ツロロツ ( 人足がいつ		14 11 COOC
				US	2002168402		
				US US	2002168402		28-11-2002
WO	0061108	A	19-10-2000	US AT	2002176935	A1 T	28-11-2002 
WO	0061108	A	19-10-2000	US AT AU	2002176935 233084 4417500	A1 T A	28-11-2002 15-03-2003 14-11-2000
WO -	0061108	A	19–10–2000	US AT AU DE	2002176935 233084 4417500 60001492	T A D1	28-11-2002 15-03-2003 14-11-2000 03-04-2003
WO	0061108	A	19–10–2000	AT AU DE DE	233084 4417500 60001492 60001492	A1 T A D1 T2	28-11-2002 15-03-2003 14-11-2000 03-04-2003 18-12-2003
WO	0061108	A	19-10-2000	AT AU DE DE DK	233084 4417500 60001492 60001492 1169019	A1 T A D1 T2 T3	28-11-2002 15-03-2003 14-11-2000 03-04-2003 18-12-2003 02-06-2003
wo ·	0061108	A	19-10-2000	AT AU DE DE	233084 4417500 60001492 60001492	A1 T A D1 T2 T3	28-11-2002 15-03-2003 14-11-2000 03-04-2003 18-12-2003 02-06-2003 09-01-2002
WO	0061108	A	19-10-2000	AT AU DE DE DK	233084 4417500 60001492 60001492 1169019	A1 T A D1 T2 T3 A1	28-11-2002 15-03-2003 14-11-2000 03-04-2003 18-12-2003 02-06-2003
WO -	0061108	A	19-10-2000	AT AU DE DE DK EP	233084 4417500 60001492 60001492 1169019 1169019	T A D1 T2 T3 A1 T3	28-11-2002 15-03-2003 14-11-2000 03-04-2003 18-12-2003 02-06-2003 09-01-2002

normation on patent tamily members

In 31 Application No PCT/US2004/015621

Patent document dited in search report		Publication date		Patent family member(s)	Publication date
WO 0061108	Α		PT	1169019 T	31-07-2003
WO 9953901	A	28-10-1999	AT	228823 T	15-12-2002
			ΑU	755066 B2	05-12-2002
			AU	3523199 A	08-11-1999
			BR	9909736 A	19-12-2000
			CA	2328882 A1	28-10-1999
			CN	1145478 T	14-04-2004
			DE	69904312 D1	16-01-2003
			DE	69904312 T2	16-10-2003
			DK	1073417 T3	24-03-2003
			EE	200000608 A	15-08-2001
			WO	9953901 A1	28-10-1999
			EP	1073417 A1	07-02-2001
			ES	2189410 T3	01-07-2003
			HR	20000689 A1	28-02-2001
			HU	0101608 A2	28-03-2002
			ID	27887 A	03-05-2001
			JP	2002512183 T	23-04-2002
			NO	20005218 A	10-11-2000
		•	NZ	507619 A	30-05-2003
			PL	343491 A1	27-08-2001
			PT SI	1073417 T	30-04-2003
			TR	1073417 T1	31-08-2003
			US	200100144 T2 2003157032 A1	21-06-2001
			ZA	200005761 A	21-08-2003 17-10-2001
				200005761 A	17-10-2001
WO 9208447	Α	29-05-1992	ΑT	127012 T	15-09-1995
			AU	653369 B2	29-09-1994
			AU	8862991 A	11-06-1992
			CA	2094727 A1	10-05-1992
			DE	69112635 D1	05-10-1995
		4	DE	69112635 T2	08-02-1996
			DK	556239 T3	06-11-1995
			EP	0556239 A1	25-08-1993
			ES	2078550 T3	16-12-1995
			WO	9208447 A1	29-05-1992
			GR	3018171 T3	29-02-1996
			JP JP	3468767 B2	17-11-2003
				6501693 T	24-02-1994
			US	5785952 A	28-07-1998

